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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

KWON, BRIAN YONG S

ART UNIT

PAPER NUMBER

1614

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Period for Reply

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
4a) Of the above claim(s) 2-4, 11, 15 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 5-10 and 12-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 09/26/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

DETAILED ACTION

Applicants Response to Restriction Requirement Acknowledged

1. Applicant's election with (a) anti-platelet agent in combination with (c) radiation therapy as the elected species is acknowledged. Claims 1, 5-10 and 12-14 read on the elected species. Accordingly, claims 2-4, 11 and 15-16 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

Claim Objections

2. Claim 10 is objected. Incorporation by reference to a specific figure or table is not permitted unless there is absolutely no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a table in the claim. In this case, the claim fails to meet the criteria mentioned above. In addition, claim 10 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n).

4. The claims 13 and 14 are objected of being redundant in describing identical compounds. For example, Brand name drugs, Reopro (Brand name), Arixtra, Novastan, and Streptas, refer to the same compound, abciximab, fondaparinux sodium, argatroban and streptokinase, respectively.

4. Claim 5 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 6. The American Heritage Dictionary (Second College Edition, 1982) defines "concurrent" as "happening at the same time". The word "simultaneous" is defined as "happening, existing, or done at the same time". As discussed in preceding comments, both terms "concurrently" and "simultaneously" have the same meaning.

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When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 5-10 and 12-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the specific proliferative disease (e.g., glioma and lung carcinoma), does not reasonably provide enablement for treating “a proliferative disease” or “diseases set forth in Table 1”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

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When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The claims are directed to a method for treating proliferative diseases comprising administering anti-platelet agent in combination with radiation therapy.

There are no known compounds of similar structure which have been demonstrated to treat all types of proliferative disease. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a “silver bullet” is contrary to our present understanding of pharmacology.

For example, different types of cancers which characterized by proliferation of cells affect different organs and have different method of growth and harm the body. Cecil Textbook of Medicine states that “each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study” (see the enclosed article, page 1004). Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein ‘evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers’. Thus, it is beyond the skill of oncologists today to get an agent to be effective against all proliferative disease.

The relative skill of those in the art of pharmaceuticals and unpredictability in the pharmaceutical art is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds for the scope of the claimed invention. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of

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enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The instant claims embrace the treatment of any disease related to cell proliferation. The instant claims cover glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, insulin-dependent diabetes mellitus (Type I), autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, or graft vs. host disease, myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, or multiple myeloma, acute pancreatitis, chronic pancreatitis, asthma, allergies, or adult respiratory distress syndrome, psoriasis and rheumatoid arthritis, proliferative cardiovascular diseases, such as restenosis, proliferative ocular disorders, such as diabetic retinopathy and macular degeneration, and benign hyperproliferative diseases, such as benign prostatic hypertrophy, hemangiomas and other cancers.

The specification discloses assays, in vitro or vivo, of testing the activity of clopidogrel on U-87 glioblastoma cells and A-549 non-small cell lung cancer cells and provides that treatment of clopidogrel alone or in combination with radiation results in delaying of tumor growth. However, there is no demonstrated correlation that the tests and results apply to all of the disorders embraced by the instant claims.

Since the efficacy of using said combination in treating various types of diseases or conditions related to proliferation of cells cannot be predicted from a priori but must be

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determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 10, 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 and 14 contain the trademark/trade name Plavix, Reopro, Arixtra, Novastan, Steptase, Ticlid, Retavase, Activase, TNKase, Integrilin, Innohep and etc... Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe clopidogrel, abciximab, fondaparinux sodium, argatroban, streptokinase, ticlopidine, reteplase, alteplase, tenecteplase, eptifibatide, tinzaparin and etc... and, accordingly, the identification/description is indefinite.

Regarding claim 10, claim 10 recites the term “proliferative disease is selected from the diseases set forth in Table 1”. Although the specific embodiments are shown in the specification (Table 1), it is considered that the meaning of the claims should be clear from the wording of the claim alone. Thus, claim 10 is vague and unclear and leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

For the examination purpose, the claimed invention is interpreted as the same scope as the claimed 1 invention, “a proliferative disease”.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 7, 8, 12, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Waksman et al. (Circulation, 2001; 103:2332-2335).

Waksman teaches the use of intracoronary radiation with the administration of antiplatelet therapy such as clopidogrel (Plavix) in treating patient with in-stent restenosis (abstract and Table 1), wherein clopidogrel is administered sequentially to the patient receiving radiation therapy (Methods).

Since the referenced restenosis (metes and bounds the broadly defined “proliferative disease”, the reference anticipates the claimed invention.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 5, 6, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waksman et al. (Circulation, 2001; 103:2332-2335).

The teaching of Waksman has been discussed in above 35 USC 102(b) rejection.

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The teaching of Waksman differs from the claimed invention in the administration of said combination in “concurrently”, “simultaneously” or “said anti-platelet agent is administered first”.

However, those of ordinary skill in the art would have been readily optimized effective concurrent administration regimens as determined by good medical practice and the clinical condition of the individual patient. Determination of the appropriate order of administration regimen for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation.

Generally, differences in time will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such time difference is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable time ranges by routine experimentation.

Conclusion

9. No Claim is allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

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Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov> Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
Patent Examiner
AU 1614

A handwritten signature in black ink, appearing to be 'B. Kwon', followed by a long horizontal line extending to the right.